SEQUENCE LISTING

- (1) GENERAL INFORMATION:
 - (i) APPLICANT: Lin, Lih-Ling Graham, James
 - (ii) TITLE OF INVENTION: NOVEL INTERLEUKIN-1 RECEPTOR INTRACELLULAR LIGAND PROTEINS AND INHIBITORS OF LIGAND
 - (iii) NUMBER OF SEQUENCES: 7
 - (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: LEGAL AFFAIRS, GENETICS INSTITUTE, INC.(B) STREET: 87 CambridgePark Drive

 - (C) · CITY: Cambridge
 - (D) STATE: MA
 - (E) COUNTRY: USA
 - (F) ZIP: 02140
 - (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
 - (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER: (B) FILING DATE:

 - (C) CLASSIFICATION:
 - (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Brown, Scott A.
 - (B) REGISTRATION NUMBER: 32,724
 - (C) REFERENCE/DOCKET NUMBER: GI5258
 - (ix) TELECOMMUNICATION INFORMATION:
 - ···(A) TELEPHONE: (617) 498-8224
 - (B) TELEFAX: (617) 876-5851
- (2) INFORMATION FOR SEQ ID NO:1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1571 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..529
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
- G ATC CCC AGG GTG GAC CTC CGG GTG TGG CAG GAC TGC TGT GAA GAC Ile Pro Arg Val Asp Leu Arg Val Trp Gln Asp Cys Cys Glu Asp 10 1

45

	r AGG s Arg															94
AG. Ar	A CGG g Arg	TCT Ser	CTT Leu 35	GAG Glu	TTC Phe	AGC Ser	TAC Tyr	CAG Gln 40	GAG Glu	GAC Asp	AAG Lys	CCG Pro	ACC Thr 45	AAG Lys	AAA Lys	142
	A AGA r Arg															190
	C AAC r Asn 65															238
AA As 8	r GAC n Asp 0	TTC Phe	AGA Arg	GAG Glu	TTT Phe 85	GTT Val	CTG Leu	GAA Glu	ATG Met	CAG Gln 90	AAG Lys	ACC Thr	ATC Ile	ACA Thr	GAC Asp 95	286
CT Le	C AGA u Arg	ACA Thr	CAG Gln	ATA Ile 100	AAG Lys	AAA Lys	CTT Leu	GAA Glu	TCA Ser 105	CGG Arg	CTC Leu	AGT Ser	ACC Thr	ACA Thr 110	GAG Glu	334
TG Cy	C GTG s Val	GAT Asp	GCC Ala 115	GGG Gly	GGC Gly	GAA Glu	TCT Ser	CAC His 120	GCC Ala	AAC Asn	AAC Asn	ACC Thr	AAG Lys 125	TGG Trp	AAA Lys	382
AA Ly	A GAT s Asp	GCA Ala 130	TGC Cys	ACC Thr	ATT Ile	TGT Cys	GAA Glu 135	TGC Cys	AAA Lys	GAC Asp	GGG Gly	CAG Gln 140	GTC Val	ACC Thr	TGC Cys	430
TT Ph	C GTG e Val 145	Glu	GCT Ala	TGC Cys	CCC Pro	CCT Pro 150	GCC Ala	ACC Thr	TGT Cys	GCT Ala	GTC Val 155	CCC Pro	GTG Val	AAC Asn	ATC Ile	478
CC Pr 16	A GGG o Gly	GCC Ala	TGC Cys	TGT Cys	CCA Pro 165	GTC Val	TGC Cys	TTA Leu	CAG Gln	AAG Lys 170	Arg	GCG Ala	GAG Glu	GAA Glu	AAG Lys 175	526
CC	C TAG		CTG	GGAG	GCTC	CT C	AGAG	TTTG	T CT	GCTG	TGCC	ATC	GTGA	GAT		579
CG	GGTGG	CCG	ATGG	CAGG	GA G	CTGC	GGAC	T GC	AGAC	CAGG	AAA	CACC	CAG	AACT	CGTGAC	639
ΑT	TTCAT	GAC	AACG	TCCA	GC T	GGTG	CTGT	T AC	AGAA	GGCA	GTG	CAGG	AGG	CTTC	CAACCA	,699 .'
GA	GCATC	TGC	GGAG	AAGG	AG G	CACA	GCAG	G TG	CCTG	AAGG	GAA	GCAG	GCA	GGAG	TCCTAG	759
CI	TCACG	ATT	GACT	TCTC	AG G	TTTT	TATT	T AA	TTCT	TTTA	. AAA	TGAA	AAA	TTGG	TGCTAC	819
TA	AAATT.	TTG	CACA	GTTG	AA T	CATT	TAGG	C GC	CTAA	ATTG	ATT	TTGC	CTC	CCAA	CACCAT	879
ТТ	CTTTT	TAA	ATAA	AGCA	.GG A	TACC	TCTA	TA T	'GTCA	GCCT	TGC	CTTC	TTC	AGAT	GCCAGG	939
															CTCACC	999
															ACGGAA	1059
															CCCCCG	
															TTCACC	
AC	ACGTO	CAGC	ATCI	CTAA	CCC P	AGAC	AAAC	CA TI	CCCG	CTGC	TCC	BAAGO	CAGC	TGT	TAGCCT	
C	יכים כיייכ	יייירר	CTCT	יכיירים	GC 1	ጉጥጋጋን	יככאַר	'A CC	TGAT	TAGA	ACA	ATTC	AATA	GCCA	CATTTA	1299

GAAACAGGTT	TGCTTTCAGC	TGTCACTTGC	ACACATACTG	CCTAGTTGTG	AACCAAATGT	1359
GAAAAAACCT	CCTTCATCCC	ATTGTGTATC	TGATACCTGC	CGAGGGCCAA	GGGTGTGTGT	1419
TGACAACGCC	GCTCCCAGCC	GGCCCTGGTT	GCGTCCACGT	CCTGAACAAG	AGCCGCTTCC	1479
GGATGGCTCT	TCCCAAGGGA	GGAGGAGCTC	AAGTGTCGGG	AACTGTCTAA	CTTCAGGTTG	1539
TGTGAGTGCG	ТТААААААА	ааааааааа	AA			1571

- (2) INFORMATION FOR SEQ ID NO:2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 176 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MÔLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ile Pro Arg Val Asp Leu Arg Val Trp Gln Asp Cys Cys Glu Asp Cys

1 10 15

Arg Thr Arg Gly Gln Phe Asn Ala Phe Ser Tyr His Phe Arg Gly Arg
20 25 30

Arg Ser Leu Glu Phe Ser Tyr Gln Glu Asp Lys Pro Thr Lys Lys Thr 35 40 45

Arg Pro Arg Lys Ile Pro Ser Val Gly Arg Gln Gly Glu His Leu Ser 50 60

Asn Ser Thr Ser Ala Phe Ser Thr Arg Ser Asp Ala Ser Gly Thr Asn 65 70 75 80

Asp Phe Arg Glu Phe Val Leu Glu Met Gln Lys Thr Ile Thr Asp Leu 85 90

Arg Thr Gln Ile Lys Lys Leu Glu Ser Arg Leu Ser Thr Thr Glu Cys 100 105

Val Asp Ala Gly Gly Glu Ser His Ala Asn Asn Thr Lys Trp Lys Lys 115 120 125

Asp Ala Cys Thr Ile Cys Glu Cys Lys Asp Gly Gln Val Thr Cys Phe 130 135 140

Val Glu Ala Cys Pro Pro Ala Thr Cys Ala Val Pro Val Asn Ile Pro 145 150 155 160

Gly Ala Cys Cys Pro Val Cys Leu Gln Lys Arg Ala Glu Glu Lys Pro 165 170 175

- (2) INFORMATION FOR SEQ ID NO:3:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1088 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..961

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

((xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:															
Lys	G AAA AAA GGA GGT AAA ACA GAA CAG GAT GGC TAT CAG AAA CCC ACC Lys Lys Gly Gly Lys Thr Glu Gln Asp Gly Tyr Gln Lys Pro Thr 1 5													46		
AAC A Asn I	AAA Lys	CAC His	TTC Phe	ACG Thr 20	CAG Gln	AGT Ser	CCC Pro	AAG Lys	AAG Lys 25	TCA Ser	GTG Val	GCC Ala	GAC Asp	CTG Leu 30	CTG Leu	94
GGG I																142
GCT G Ala G																190
TTC T																238
CCT G Pro V 80																286
GAG A									_							334
CTC A		Ser														382
TTC A	ATG	GTG								_		_				430
GTA C Val F																478
TCC C Ser A 160																526
AAA C	GAG Glu	GAA Glu	GTT Val	GGG Gly 180	GGA Gly	GTG Val	TTA Leu	GAA Glu	CTG Leu 185	TTC Phe	CCA Pro	ATT Ile	AAT Asn	GGG Gly 190	AGC Ser	574
TCT (GTT Val	GTT Val	GAG Glu 195	CGA Arg	GAA Glu	GAC Asp	GTA Val	CCA Pro 200	GCC Ala	CAT His	TTG Leu	GTG Val	AAA Lys 205	GAC Asp	ATT Ile	622
CGT A																670
GGA A	AAA Lys 225	GAC Asp	GGA Gly	AAT Asn	GTC Val	AAA Lys 230	TCC Ser	TGG Trp	TAT Tyr	CCT Pro	TCC Ser 235	CCA Pro	ATG Met	TGG Trp	TCC Ser	718

ATG Met 240																766
GAA Glu	ATG Met	GCG Ala	ATT Ile	CAG Gln 260	CAG Gln	TCA Ser	CTG Leu	GGG Gly	ATG Met 265	CGC Arg	TGC Cys	CAG Gln	AAG Lys	ATG Met 270	AGT Ser	814
ATG Met	CAG Gln	GCT Ala	ATG Met 275	GTT Val	ACC Thr	ATA Ile	GTT Val	ACC Thr 280	ACC Thr	AAG Lys	GAT Asp	ACC Thr	AGG Arg 285	ATG Met	GTT Val	862
					GTC Val										CTT Leu	910
					GTA Val											958
TGC Cys 320	TAAA	ACTI	ACA 1	rgtg(GCÇA(GC TO	CCAT'	rctt(C CA	CACT	GCGT	ACT	ACAT"	rtc		1011
CTGC	CTT	CTT (CTTT	CAGT	GT T	rttc:	raag:	A CT	AAAT	TAAA	AGC	AAAC'	TTT	CACC'	AAAAA	1071
AAAA	IAAA	AAA A	AAAA	AAA												1088

- (2) INFORMATION FOR SEQ ID NO:4:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 320 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Lys Lys Gly Gly Lys Thr Glu Gln Asp Gly Tyr Gln Lys Pro Thr Asn 1 10 15

Lys His Phe Thr Gln Ser Pro Lys Lys Ser Val Ala Asp Leu Leu Gly 20 25 30

Ser Phe Glu Gly Lys Arg Arg Leu Leu Leu Ile Thr Ala Pro Lys Ala 35 40 45

Glu Asn Asn Met Tyr Val Gln Gln Arg Asp Glu Tyr Leu Glu Ser Phe 50 60

Cys Lys Met Ala Thr Arg Lys Ile Ser Val Ile Thr Ile Phe Gly Pro 65 70 75 80

Val Asn Asn Ser Thr Met Lys Ile Asp His Phe Gln Leu Asp Asn Glu $90 \hspace{1.5cm} 95$

Lys Pro Met Arg Val Val Asp Asp Glu Asp Leu Val Asp Gln Arg Leu 100 105 110

Ile Ser Glu Leu Arg Lys Glu Tyr Gly Met Thr Tyr Asn Asp Phe Phe 115 120 125

Met Val Leu Thr Asp Val Asp Leu Arg Val Lys Gln Tyr Tyr Glu Val 130 135 140

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Pro 145	Ile	Thr	Met	Lys	Ser 150	Val	Phe	Asp	Leu	11e 155	Asp	Thr	Phe	Gin	Ser 160	
Arg	Ile	Lys	Asp	Met 165	Glu	Lys	Gln	Lys	Lys 170	Glu	Gly	Ile	Val	Cys 175	Lys	
Glu	Glu	Val	Gly 180	Gly	Val	Leu	Glu	Leu 185	Phe	Pro	Ile	Asn	Gly 190	Ser	Ser	
Val '	Val	Glu 195	Arg	Glu	Asp	Val	Pro 200	Ala	His	Leu	Val	Lys 205	Asp	Ile	Arg	
Asn	Tyr 210	Phe	Gln	Val	Ser	Pro 215	Glu	Tyr	Phe	Ser	Met 220	Leu	Leu	Val	Gly	•
Lys 225	Asp	Gly	Asn	Val	Lys 230	Ser	Trp	Tyr	Pro	Ser 235	Pro	Met	Trp	Ser	Met 240	
Val	Ile	Val	Tyr	Asp 245	Leu	Ile	Asp	Ser	Met 250	Gln	Leu	Arg	Arg	Gln 255	Glu	
Met	Ala	Ile	Gln 260	Gln	Ser	Leu	Gly	Met 265	Arg	Cys	Gln	Lys	Met 270	Ser	Met	
Gln	Ala	Met 275	Val	Thr	Ile	Val	Thr 280	Thr	Lys	Asp	Thr	Arg 285	Met	Val	Thr	
Arg	Met 290	Thr	Thr	Val	Ile	Met 295	Arg	Val	Ile	Thr	Met 300	Asp	Thr	Leu	Thr	
Glu 305	Gln	Lys	Tyr	Val	Thr 310	Leu	Asp	Ser	Ala	Ser 315	Phe	Leu	Cys	Ser	Cys 320	
	(i) (11) (i1i) (ix) SE((1 (1 (1 (1)) MO:) HY:) FE. (1	QUENCA) L B) T C) S D) T LECU POTH ATUR A) L	CE CE ENGTE YPE: TRAN. OPOL. LE TETICE E: TAME/OCAT	SEQ HARAGH: 1 nuc DEDN: OGY: YPE: AL: KEY: ION:	CTER 759 leic ESS: lin cDN NO	ISTICOASE ACTO	CS: pai d ble		O:5:						,
									la A					AC A Lsp T		46
TTC Phe	ATC Ile	AAC Asn	CTC Leu	CGG Arg 20	Glu	GTG Val	CTC Leu	AAC Asn	CGC Arg 25	Phe	AAG Lys	CTG Let	CCG Pro	002 229 30	GGA Gly	94
GAG Glu	TAC Tyr	ATT Ile	CTC Leu	ı Val	CCT Pro	TCC Ser	ACC Thr	TTC Phe	Glu	CCC	AAC Asn	AAC Lys	GAT Asp	gl;	GAT Asp	142

TTC Phe	TGC Cys	Ile 50	Arg	Val	Phe	Ser	GAA Glu 55	AAG Lys	Lys	Ala	Asp	Tyr 60	Gln	Ala	Val	190
GAT Asp	GAT Asp 65	GAA Glu	ATC Ile	GAG Glu	GCC Ala	AAT Asn 70	CTT Leu	GAA Glu	GAG Glu	TTC Phe	GAC Asp 75	ATC Ile	AGC Ser	GAG Glu	GAT Asp	238
GAC Asp 80	ATT Ile	GAT Asp	GAT Asp	GGA Gly	TTC Phe 85	AGG Arg	AGA Arg	CTG Leu	TTT Phe	GCC Ala 90	CAG Gln	TTG Leu	GCA Ala	GGA Gly	GAG Glu 95	286
				TCT Ser 100												334
				CAA Gln												382
				GTT Val							_				CTG Leu	≟ 30
_				TTC Phe											CAA Gln	1 78
				GAA Glu												526
				AAG Lys 180											TGT Cys	5~€
	Leu			GTC Val											ATC Ile	€22
															CTA Leu	€_0
															GAG Glu	-19
				TCT Ser									AGTT.	ATA		' ~6 4
ACT.	AATC'	TGC	CTGA	AGAC'	TT C	TCAT	GATG	g aa	AATC	AGCC	AAG	GACT	AAG	CTTC	CATAGA	824
AAT.	ACAC'	TTT	GTAT	CTGG.	AC C	TCAA	AATT	A TG	GGAA	CATT	TAC	TTAA	ACG	GATG	ATCATA	884
GCT	gaaa.	ATA .	ATGA	TACT	GT C	AATT	TGAG	A TA	GCAG	AAGT	TTC	ACAC	ATC	AAAG	TAAAAG	944
ATT	TGCA	TAT	CATT	ATAC	TA A	ATGC	AAAT	G AG	TCGC	AATT	CCC	TTGA	CAA	GGTC	AAAGAA	1004
AGC [*]	TTTA	TAA	CTGT	TAAA	AG T	ATAC	ACTT	т тт	ACTT	TTAC	ACA	CTTT	CCT	GTTC	ATAGCA	106-
ATA	TTAA	ATC	AGGA	AAAA	AA A	ATGC	AGGG	A GG	TATT	TAAC	AGC	TGAG	CAA	AAAC	ATTGAG	112.
TCG	CTCT	CAA	AGGA	.CACG	AG G	CCCT	TGGC	A GG	GAAT	TTTA	' AAA	.GCAA	CT'l'	CAAG	TTTAAA	118.
ATG	CAGC	TGT	TGAT	TCTA	CC A	AACA	ACAG	T CC	'AAGA	TTAC	CAT	TTCC	CAT	GAGC	CAACTG	124

GGAAACATGG	TATATCATGA	AGTAATCTTG	TCAAGGCATC	TGGAGAGTCC	AGGAGAGAG	1304
ACTCACCTCT	GTCGCTTGGG	TTAAACAAGA	GACAGGTTTT	GTAGAATATT	GATTGGTAAT	1364
AGTAAATCGT	TCTCCTTACA	ATCAAGTTCT	TGACCCTATT	CGGCCTTATA	CATCTGGTCT	1424
TACAAAGACC	AAAGGGATCC	TGCGCTTGAT	CAACTGAACC	AGTATGCCAA	AACCAGGCAT	1484
CCAATTTGTA	AACCAATTAT	GATAAAGGAC	AAAATAAGCT	GTTTGCCACC	TCAAAACTTT	1544
ATGAACTTCA	CCACCACTAG	TGTCTGTCCA	TGGAGTTAGA	GGGGACATCA	CTTAGAAGTT	1604
CTTATAGAAA	GGACACAAGT	TTGTTTCCTG	GCTTTACCTT	GGGAAAATGC	TAGCAACATT	1664
ATAGAAATTT	TGCCTTGTTG	CCTTATCTTC	TTCCAAATGT	ACTGTTAAAT	AAAAATAAAG	172
GGTTACCCCA	TGCAATCAAA	ААААААААА	AAAAA			175

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 251 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Lys Asn Phe Phe Leu Thr Asn Arg Ala Arg Glu Arg Ser Asp Thr Phe 1 5 10

Ile Asn Leu Arg Glu Val Leu Asn Arg Phe Lys Leu Pro Pro Gly Glu 20 25 30

Tyr Ile Leu Val Pro Ser Thr Phe Glu Pro Asn Lys Asp Gly Asp Phe 35 40 45

Cys 4le Arg Val Phe Ser Glu Lys Lys Ala Asp Tyr Gln Ala Val Asp 50 60

Asp Glu Ile Glu Ala Asn Leu Glu Glu Phe Asp Ile Ser Glu Asp Asp 65 70 75 80

Ile Asp Asp Gly Phe Arg Arg Leu Phe Ala Gln Leu Ala Gly Glu Asp 85 90 95

Ala Glu Ile Ser Ala Phe Glu Leu Gln Thr Ile Leu Arg Arg Val Leu 100 105 110

Ala Lys Arg Gln Asp Ile Lys Ser Asp Gly Phe Ser Ile Glu Thr Cys 115 120

Lys Ile Met Val Asp Met Leu Asp Ser Asp Gly Ser Gly Lys Leu Gly 130 135

Leu Lys Glu Phe Tyr Ile Leu Trp Thr Lys Ile Gln Lys Tyr Gln Lys 145 \$150\$

Ile Tyr Arg Glu Ile Asp Val Asp Arg Ser Gly Thr Met Asn Ser Tyr 165 170 175

Glu Met Arg Lys Ala Leu Glu Glu Ala Gly Phe Lys Met Pro Cys Gln 180 185 190 Leu His Gln Val Ile Val Ala Arg Phe Ala Asp Asp Gln Leu Ile Ile 195 200 205

Asp Phe Asp Asn Phe Val Arg Cys Leu Val Arg Leu Glu Thr Leu Phe 210 215 220

Lys Ile Phe Lys Gln Leu Asp Pro Glu Asn Thr Gly Thr Ile Glu Leu 225 230 240

Asp Leu Ile Ser Trp Leu Cys Phe Ser Val Leu 245 250

- (2) INFORMATION FOR SEQ ID NO:7:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 700 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE; protein
 - (iii) HYPOTHETICAL: NO
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:
 - Met Ala Gly Ile Ala Ala Lys Leu Ala Lys Asp Arg Glu Ala Ala Glu
 1 5 10
 - Gly Leu Gly Ser His Glu Arg Ala Ile Lys Tyr Leu Asn Gln Asp Tyr
 20 25 30
 - Glu Ala Leu Arg Asn Glu Cys Leu Glu Ala Gly Thr Leu Phe Gln Asp 35 40 45
 - Pro Ser Phe Pro Ala Ile Pro Ser Ala Leu Gly Phe Lys Glu Leu Gly 50 60
 - Pro Tyr Ser Ser Lys Thr Arg Gly Met Arg Trp Lys Arg Pro Thr Glu 65 70 75 80
 - Ile Cys Ala Asp Pro Gln Phe Ile Ile Gly Gly Ala Thr Arg Thr Asp 85 90 95
 - Ile Cys Gln Gly Ala Leu Gly Asp Cys Trp Leu Leu Ala Ala Ile Ala 100 105 110
 - Ser Leu Thr Leu Asn Glu Glu Ile Leu Ala Arg Val Val Pro Leu Asn 115 120 125
 - Gln Ser Phe Gln Glu Asn Tyr Ala Gly Ile Phe His Phe Gln Phe Trp 130 135
 - Gln Tyr Gly Glu Trp Val Glu Val Val Val Asp Asp Arg Leu Pro Thr 145 150 155 160
 - Lys Asp Gly Glu Leu Leu Phe Val His Ser Ala Glu Gly Ser Glu Pne 165 170 175
 - Trp Ser Ala Leu Leu Glu Lys Ala Tyr Ala Lys Ile Asn Gly Cys Tyr 180 185 190
 - Glu Ala Leu Ser Gly Gly Ala Thr Thr Glu Gly Phe Glu Asp Phe Thr 195 200 205

Gly Gly Ile Ala Glu Trp Tyr Glu Leu Lys Lys Pro Pro Pro Asn Leu Phe Lys Ile Ile Gln Lys Ala Leu Gln Lys Gly Ser Leu Leu Gly Cys Ser Ile Asp Ile Thr Ser Ala Ala Asp Ser Glu Ala Ile Thr Phe Gln Lys Leu Val Lys Gly His Ala Tyr Ser Val Thr Gly Ala Glu Glu Val Glu Ser Asn Gly Ser Leu Gln Lys Leu Ile Arg Ile Arg Asn Pro Trp Gly Glu Val Glu Trp Thr Gly Arg Trp Asn Asp Asn Cys Pro Ser Trp Asn Thr Ile Asp Pro Glu Glu Arg Glu Arg Leu Thr Arg Arg His Glu 310 315 Asp Gly Glu Phe Trp Met Ser Phe Ser Asp Phe Leu Arg His Tyr Ser 325 330 Arg Leu Glu Ile Cys Asn Leu Thr Pro Asp Thr Leu Thr Ser Asp Thr Tyr Lys Lys Trp Lys Leu Thr Lys Met Asp Gly Asn Trp Arg Arg Gly Ser Thr Ala Gly Gly Cys Arg Asn Tyr Pro Asn Thr Phe Trp Met Asn Pro Gln Tyr Leu Ile Lys Leu Glu Glu Glu Asp Glu Asp Glu Glu Asp Gly Glu Ser Gly Cys Thr Phe Leu Val Gly Leu Ile Gln Lys His Arg 405 410 415 Arg Arg Gln Arg Lys Met Gly Glu Asp Met His Thr Ile Gly Phe Gly Ile Tyr Glu Val Pro Glu Glu Leu Ser Gly Gln Thr Asn Ile His Lei Ser Lys Asn Phe Phe Leu Thr Asn Arg Ala Arg Glu Arg Ser Asp Thr Phe Ile Asn Leu Arg Glu Val Leu Asn Arg Phe Lys Leu Pro Pro Gly Glu Tyr Ile Leu Val Pro Ser Thr Phe Glu Pro Asn Lys Asp Gly Asp 485 490 Phe Cys Ile Arg Val Phe Ser Glu Lys Lys Ala Asp Tyr Gln Ala Val 500 505 Asp Asp Glu Ile Glu Ala Asn Leu Glu Glu Phe Asp Ile Ser Glu Asp 520 Asp Ile Asp Asp Gly Val Arg Arg Leu Phe Ala Gln Leu Ala Gly Glu Asp Ala Glu Ile Ser Ala Phe Glu Leu Gln Thr Ile Leu Arg Arg Val 550 555

Leu Ala Lys Arg Gln Asp Ile Lys Ser Asp Gly Phe Ser Ile Glu Thr \$565\$ \$570\$ \$575

Cys Lys Ile Met Val Asp Met Leu Asp Ser Asp Gly Ser Gly Lys Leu 580 585 590

Gly Leu Lys Glu Phe Tyr Ile Leu Trp Thr Lys Ile Gln Lys Tyr Gln $595 \hspace{1.5cm} 600 \hspace{1.5cm} 605$

Lys Ile Tyr Arg Glu Ile Asp Val Asp Arg Ser Gly Thr Met Asn Ser 610 $\,$ 620 $\,$

Tyr Glu Met Arg Lys Ala Leu Glu Glu Ala Gly Phe Lys Met Pro Cys 625 630 635

Gln Leu His Gln Val Ile Val Ala Arg Phe Ala Asp Asp Gln Leu Ile 645 650 655

Ile Asp Phe Asp Asn Phe Val Arg Cys Leu Val Arg Leu Glu Thr Leu 660 665 670

Phe Lys Ile Phe Lys Gln Leu Asp Pro Glu Asn Thr Gly Thr Ile Glu 675 680 685

Leu Asp Leu Ile Ser Trp Leu Cys Phe Ser Val Leu 690 695 700